DIAGNOSTIC ACCURACY OF ENDOMETRIAL CURETTAGE IN COMPARISON TO HYSTERECTOMY SPECIMENS IN PATIENTS WITH ABNORMAL UTERINE BLEEDING

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ABSTRACT

Background

Endometrial biopsy is an important technique used in the assessment of the Abnormal Uterine Bleeding (AUB) in women >40 years and post-menopausal women to exclude endometrial pathological abnormalities (endometrial hyperplasia and carcinoma) and confirm benign nature of the problem. Patients will be offered conservative or medical treatment and unnecessary radical surgery can be avoided.

Objectives

To compare the diagnostic accuracy of endometrial curetting and the subsequent hysterectomy specimen histology in AUB in women > 40 years old and postmenopsal women. Also to evaluate causes of per and post-menopausal bleeding.

Patients and Methods

Endometrial sampling was obtained by dilatation and curetting (D&C) on 80 patients in premenopausal and post-menopausal women. Most of those patients were already planned for hysterectomy for abnormal uterine bleeding. Verbal consent was taken from all patients. Both samples were numbered and sent to a different histolopathologist. The histology report of both D&C and hysterectomy specimens were compared. Hysterectomy report was considered as the gold standard.

Results

Mean duration between the curetting and hysterectomy was 5 weeks. The histology of 80 samples obtained by D&C show normal endometrium in 25 cases, endometrial hyperplasia without atypia in 36 specimens and with atypia in 4 specimens, endometrial polyps in 10, atrophic endometrium in one specimen, and endometrial carcinoma in 3 specimens. 98.8% of the samples obtained by D&C were adequate for histological examination. Our results show 77.5% of the cases concordance between the D&C and hysterectomy specimen. Accuracy for complex hyperplasia with or without atypical was 100% sensitivity, 100% specificity, followed by simple hyperplasia and benign endometrial causes of AUB condition.

Conclusion

Abnormal Uterine Bleeding AUB increases with age, with a profound increase in incidence in premenopausal women. Endometrial hyperplasia was the most common cause of AUB. D&C is an accurate, minimally invasive procedure for detecting endometrial pathology especially for complex hyperplasia, and it has high sensitivity and specificity than those of simple hyperplasia.

Keywords: *Abnormal uterine bleeding, Endometrial biopsy, D&C, Hysterectomy* .

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INTRODUCTION

Abnormal Uterine Bleeding (AUB) is any variation from the normal menstrual cycle, and includes changes in regularity and frequency of menses, in duration of flow, or in amount of blood loss [1]. Abnormal uterine bleeding is a major gynecological problem, accounting for 33% of outpatient referrals, including 69% of referrals in the perimenopausal and postmenopausal age groups [2]. The prevalence of AUB is difficult to determine, however, 9 to 30% of women of reproductive age have menstrual irregularities requiring medical evaluation [3].

Evaluation of the abnormal uterine bleeding in any women of more than 40 years or menopausal women is of critical importance to confirm the benign nature of the problem and to exclude endometrial carcinoma, so that medical or conservative treatment can be offered and unnecessary radical surgery can be avoided [4].The main aim of investigation for AUB is to exclude intra uterine pathology, Particularly endometrial cancer [5].

Endometrial tissue sampling is one of the most common diagnostic procedure in the assessment of women with abnormal uterine bleeding .The endometrium is a dynamic tissue with physiological and characteristic morphological changes during the menstrual cycle as a result of the sex steroid hormones produced in the ovary [6].

Abnormal uterine bleeding in perimenopause includes the period beginning with the first clinical, biological and endocrinological features of the approaching menopause. By WHO is the period 2-8 years preceding menopause and one year after the final menses. No progesterone secreted by the ovary. Therefore the premenopausal menstrual cycles are shortened, often anovulatory and irregular [7,8].

The term postmenopausal bleeding (PMB) refers to any vaginal bleeding in a postmenopausal woman [9]. PMB is the most common reason for referral to gynecological rapid access clinics. Strategies for the investigation and treatment of women presenting with PMB have evolved since the early 1990s with the advent of transvaginal ultrasound (TVUS) and outpatient hysteroscopy. Bleeding after menopause typically originates from benign disease [10] . After the menopause, endometrial thickening may be indicative of proliferation, cystic atrophy, simple hyperplasia, complex hyperplasia, hyperplasia with atypia, or endometrial cancer [11]. However, the ultrasound appearance of an apparently thickened endometrium may actually represent abnormalities within the endometrium or underlying myometrium such as endometrial polyps, submucous fibroids, adenomyosis or intrauterine adhesions.

Endometrial hyperplasia is irregular proliferation of the endometrial glands with an increase in the gland to stroma ratio when compared with proliferative endometrium .The incidence of endometrial hyperplasia is estimated to be at least three times higher than endometrial cancer and if left untreated it can progress to cancer [12]. Endometrial hyperplasia develops when estrogen, stimulates endometrial cell growth by binding to estrogen receptors in the nuclei of endometrial cells. This can be from endogenous or exogenous sources [13].

Endometrial hyperplasia usually occurs during perimenopause, when ovulation may not occur regularly [14]. Endometrial hyperplasia classified into simple and complex hyperplasia based on the complexity and crowding of the glandular framework [12].

Endometrial carcinoma: Endometrial cancer (EC) is the most common gynecologic malignancy; Although relatively uncommon in reproductive-aged women, It is most commonly occurs after the age of 50 and prognosis depend on the stage of the disease at the time of diagnosis. The overall life time risk of developing EC is approximately 2.5%. Most commonly (90%) EC presents with abnormal vaginal bleeding or discharge [15]. There are a large number of risk factors including unopposed estrogenic stimulation of the uterus [16].

PATIENTS AND METHODS

It's a prospective comparative study of eighty perimenopause and postmenopausal women with abnormal uterine bleeding, over a period of six months from first of September 2016 to the end of February 2017. Ethical permission was taken from scientific committee in Sulaimani Maternity Teaching Hospital for conducting this study and Informed consent was taken from the patients and documented.

Inclusion criteria included all patients with abnormal uterine bleeding in perimenopausal and Postmenopausal women not responding to medical therapy, who planned for abdominal hysterectomy age more than 40 years old was included in this study. Exclusion criteria included : Patients with pregnancy related bleeding, those with hormone producing ovarian tumor, those on HRT, those on hormone therapy like tamoxifen, or on anticoagulant and having bleeding disorder and those who have bleeding related to benign condition

diagnosed on ultrasound or MRI like fibroid and adenomyosis were excluded.

The endometrial sample was taken under Anesthesia. The procedure was typically performed in the dorsal lithotomy position; thorough clinical examination (bimanual examination) was done to assess the position of uterus and both adnexa under the anesthesia before beginning the dilatation and curettage procedure. Then hysterectomy was performed, both samples were sent for the different pathologist, the specimens were numbered to reduce bias. Uterine findings were grouped as benign condition other than hyperplasia which means both proliferative and secretory endometrium. Hyperplasia was classified into simple and complex hyperplasia with or without atypia, focal lesion like endometrial polyp, endometrial atrophy and endometrial carcinoma.

Statistical analysis

Data entry performed via using an excel spreadsheet, then the statistical analysis was performed by SPSS program, version 21 (IBM SPSS Statistical Package for the Social Sciences). Age, BMI, Age of menarche, and Parity were described by mean and SD (standard deviation). Then the continuous variables were grouped to be shown with other qualitative variables. For each diagnosis the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of D&C were calculated (depending on histopathology result of hysterectomy as gold standard), and then the total accuracy of D&C in general calculated. P values of < 0.05 were used as a cut off point for significance of statistical tests.

RESULTS

A total of 80 cases of total abdominal hysterectomy in perimenopausal and post menopausal women presented with abnormal uterine bleeding were included in this study. Patient's age ranged from 40-71 years. The mean age of study population was (49.1 + 5.9) years, most of them(56.3%) were seen in age group of 40-49 years, followed by (38.8%) in age group of 50-59 years, only (4.9%) were seen in the age group of 60-71. Twelve cases (15%) had normal BMI. 48 cases (60%) were overweight and 20 cases (25%) were obese (BMI>30). Parity in the present study ranged from 2 to 11, with majority 47 cases (58.8%) were grand multiparous women (more than5), 30 cases (37.5%) multiparous (p3-4) and only 2 cases (2.6%) of low parity (para 1-2). Regarding the age of menarche nearly half of the patient 36 (45.0%) had menarche at the age of 13 years with mean (12.7+0.9). Only 4 cases had history of infertility, one case had primary infertility 3 cases had 2ndary infertility for about 3 years. All information about age, BMI, parity, history of infertility and other information are given in (Table 1).

Table 2 shows the main presenting complaint. Menorrhagia was in nearly half of them 45 (56.3%). Irregular menstrual bleeding which includes menometrorrhagia and intermenstrual bleeding presented in 21 (26.3). While post menopausal bleeding was reported by 14 (17.5%) cases of studied group.

Most of the cases were of perimenopausal 66 and only 14 cases were postmenopausal. The endometrial thickness in perimenopausal women was less than 8mm in 17 cases (25.8%) and it was more than 8mm of women in 49 cases (74.2%), While in postmenopausal women endometrial thickness less than 5mm in 3 cases (21.4%) and 11 cases (78.6%) had endometrial thickness more than 5 mm, Table 5.

Table 4 shows the distribution of pathological diagnosis according to age group. 45 cases (56.3%) were in the age group (40-49) years, and 31 cases (38.8%) were in the age group (50-59) years, only 4 cases (5%) were in the age group > 60 years old. The most common pathology was simple endometrial hyperplasia in the age group 40-49 years and age group 50-59 years. In addition the most common pathology in age group > 60 years was endometrial carcinoma about (50%). all these information found in (Table4).

Table 5 shows the histological result in our study were discordant in 17 cases between hysterectomy and D&C. We only had one case of endometrial curetting was not satisfactory for histopathological report which was atrophic endometrium by hysterectomy specimen. The histological result was benign condition proliferative and secretory endometrium in 22 cases of hysterectomy and 25 cases by endometrial curetting, the results show 3 cases was discordant with the result of hysterectomy specimen.

Also for endometrial polyp 14 cases were found by hysterectomy specimens and 10 cases were showed by D&C specimens, the result was 4 cases discordant. Also in 3 cases that have atrophic endometrium by hysterectomy specimen and one case was found by D&C, the result was 2 cases discordant. In addition among 32 cases of simple hyperplasia diagnosed with D&C result 27cases confirmed on hysterectomy

specimen and 5 cases were discordant. In regard to simple hyperplasia with atypia 5 cases were found on hysterectomy specimen and 3 cases with D&C resulted in 2 cases were discordant. The result of D&C and hysterectomy for complex hyperplasia with and without atypia were comparable. 4 cases of endometrial carcinoma were found of hysterectomy specimen only one case of discordant by D&C was found to have proliferative endometrium.

The sensitivity, specificity , positive predictive value (PPV) and negative predictive value (NPV) and accuracy for D&C was calculated for all diagnoses of the histology results, after excluding one inadequate samples all shown in (table 6). The D&C was found to have a sensitivity, specificity, PPV, NPV and accuracy were 100% for diagnosing complex endometrial hyperplasia with and without atypia. Also it had 75.0% sensitivity, 100.0% specificity, 100.0% PPV, 98.7 NPV and 98.7% accuracy for diagnosing endometrial carcinoma.

Table 1. Demographic characteristics of patients with abnormal uterine bleeding Variable.

Variable		Frequency	Percentage
Hx infertility	No	76	95.0%
	Primary	1	1.3%
	Secondary	3	3.8%
Parity	Nulliparus	1	1.3%
	1-3	10	12.5%
	More than 3	69	86.3%
Menarche Age	11- 12 years	29	36.3%
	13 - 14 years	51	63.8%
Heavy Menses	Yes	45	56.3%
	No	35	43.8%
Inter mens bleeding	Yes	21	26.3%
	No	59	73.8%

Table 2. Main presenting complain and percentages.

Indications	Frequency	Percentage
Heavy Menstrual bleeding	45	56.3%
Irregular menstrual bleeding	21	26.3%
Post Menopausal Bleedings	14	17.5%

Table 3. Endometrial thickness in premenopausal and postmenopausal women.

Endometrial thickening	Frequency	Percentage
Less 8 mm	17	25.8%
8 mm and more	49	74.2%
Less 5 mm	3	21.4%
5 mm and more	11	78.6%

Table 4. The distribution of pathological diagnosis according to age group.

Histopathology	Age Group			P Value
	39 - 49 Years	49 - 59 Years	59 - 71 Years	
Benign conditions (Secretary & proliferative endometrium)	13	9	0	0.01
Simple hyperplasia	16	11	0	
Atypical simple hyperplasia	4	1	0	
Complex hyperplasia	2	2	0	
Atypical complex hyperplasia	0	1	0	
Endometrial carcinoma	2	0	2	
Atrophic endometrium	0	2	1	
Endometrial polyp	8	5	1	
Total	45	31	4	

Table 5. Comparison of results of D&C specimens with histopathology after hysterectomy.

Histopathology	HYS Frequency (%)	D &C Frequency (%)
Benign conditions (proliferative & Secretary endometrium)	22 (27.5 %)	26 (32.5%)
Simple hyperplasia	27 (33.8%)	32 (40.0%)
Atypical simple hyperplasia	5 (6.3%)	3 (3.8%)
Complex hyperplasia	4 (5.0%)	4 (5.0%)
Atypical complex hyperplasia	1 (1.3%)	0 (0.0%)
Endometrial carcinoma	4 (5.0%)	3 (3.8%)
Atrophic endometrium	3 (3.8%)	1 (1.3%)
Endometrial polyp	14 (17.5%)	10 (12.5%)
Inadequate sample	0 (0%)	1 (1.3)
Total	80 (100%)	80 (100.0%)

Table 6. The sensitivity, specificity , positive predictive value (PPV) and negative predictive value (NPV) and accuracy for D&C.

Histopathology pattern	Hystere_ ctomy	D & C		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
		Concordant	Dis-concordant					
Benign conditions &Secretary endometrium (proliferative)	22	18	4	81.0%	86.2%	68.0%	92.6%	84.8%
Simple hyperplasia	27	23	4	85.19%	82.7%	71.9%	91.5%	83.5%
Atypical simple hyperplasia	5	3	2	60.0%	100.0%	100%	97.4%	97.5%
Complex hyperplasia	4	4	0	100.%	100.0%	100%	100%	100%
Atypical complex hyperplasia	1	0	1	0%	100.0%	0%	98.7%	98.7%
Endometrial carcinoma	4	3	1	75%	100.0%	100%	98.7%	98.7%
Atrophic endometrium	3	1	2	33.3%	100.0%	100%	97.4%	97.5%
Endometrial polyp	14	10	4	71.4%	100.0%	100%	94.2%	94.9%
Total	79	62	17					

DISCUSSION

Perimenopausal and postmenopausal bleeding is a common presenting symptom in gynaecology outpatient with increase the incidence of endometrial carcinoma and hyperplasia with age, and other risk factors. Therefore for many years diagnostic curretage was used to exclude endometrial abnormality.

In current study the youngest patient was 40 years old and the oldest was 71 years old. Majority of the patients were grand multiparus (58.8%). The maximum incidence of AUB was found to be between the ages of 40-49 years (56.3%) and this agree with study of Muzaffar et al 2005 [17] the commonest age group between (41-50) years accounting of more cases as (38.6%). In our study commonest symptom was menorrhagia (56.3%), agreed with study of Muzaffar et al 2005 [17] which was (55.83%) but disagree with Khan M et al in 2011 who found polymenorrhea in (35%) [18]. Majority of patients in our study diagnosed with endometrial hyperplasia (46.25%) and they were more between 40-49 years of age. Similarly high prevalence of endometrial hyperplasia in perimenopausal age group was reported as 64.8% by Jairajpuri ZS et al [19] in 2013, and Muzaffar M et al [17] found that hyperplasia was occurred in 40% of cases which is comparable with our study.

Thus endometrial hyperplasia is a common diagnosis in perimenopausal women causing symptom of irregular or prolonged bleeding due to an ovulatory cycles. The correct diagnosis, evaluation and follow up of patients with this condition is important because of the malignancy potential [8, 12] .Simple endometrial hyperplasia was found in 33.8% making it the most common histological diagnosis observed in our study, comparable with study of Abdelazim et al 2013 [20] was (32.1%), and not agree with study of Mordan Sanam M1 et al in 2015 [21] (18.5%). In our study, D&C had 85.19% sensitivity, 82.7% specificity, accuracy 83.5% for diagnosis of simple hyperplasia, and this agreed with the study of Saadia et al [22] (2011) had 87.5% sensitivity 83.3% specificity and comparable with Mordan et al 2015 [21] had 92.3% sensitivity and 100% specificity and 98.5% accuracy for diagnosis of simple hyperplasia.

Complex hyperplasia in our study was observed in 5.0% of histologyical diagnosis and with atypia in 1.3%, while in the study by khan M et al in 2011 [18] was 2.8% and 1.0% respectively. Complex hyperplasia with and without atypia in our study had 100% sensitivity and 100% specificity, 100% PPV, 100% NPV, 100% Accuracy. This agreed with Pearl and Pitfalls study Coulter A et al.[23] reviewed 131 reports of endometrial biopsy and subsequent hysterectomy presented with DUB from January 2005 December 2009.

The cases of complex hyperplasia showed a higher concordance rate than those of simple hyperplasia, because those cases of simple hyperplasia (SH) were completely removed during the curettage, leaving behind the basal endometrium only, but the complex hyperplasia (CH) with a higher degree of proliferation were not totaly scraped out, hence giving a high degree of concordance for complex hyperplasia.Endometrial carcinoma (EC) found in 5.0% in our histological diagnosis and this was agreed with saraswathi D et al [(24)] was (4.4%) but not agreed with the lower incidence of 0.4% by Jairajpuri ZS et al [(19)] and Khan M et al [(18)], Muzaffar M et al in 2005 [(17)] (0.4%). A higher incidence was reported 7.1% by Abdelazim et al 2013 [(20)].

In our study, the D&C had 75.0% sensitivity, 100% specificity, 100% PPV, 98.7% NPV, and 98.7% accurate for diagnosing endometrial carcinoma. While in a study by Saadia et al in 2011 [(22)] had 33% sensitivity and 100% specificity for diagnosis of EC which is lower than our result. Also in study Mordan et al 2015 [(21)] had 100% sensitivity, 100% specificity which is higher than our result.

In our study, incidence of atrophic endometrium found by hysterectomy specimen 3.8% which is higher than 1.1% by Jairajpuri ZS et al [(19)] and less than the incidence was reported in other study 7% Ara S et al. 2011[(25)]. We found 33.3% sensitivity, 100% Specificity, 100% PPV, 97.4% NPV, 97.5% accuracy for diagnosing atrophic endometrium. One out of three cases was reported as inadequate for histological examination which found by hysterectomy to have atrophic endometrium. These result is comparable to the study of Mordan et al [(21)].

In this study D&C had 71.4% sensitivity, 100% specificity, 100% PPV, 94.9% NPV and 94.9% accuracy for detecting endometrial polyps, while in the study Saadia et al (2011) [(22)] had 66% sensitivity 92% specificity and of Abdelazim et al [(20)] study was 75% sensitivity, 100% specificity, 98.6% accurate for diagnosing endometrial polyps, which is comparable to our study.

In this study, D&C had 81.0% sensitivity, 86.2% specificity, 68.0% PPV, 92.6% NPV and 84.4% accuracy for diagnosing benign endometrium (proliferative and secretory endometrium). In the study of Saadia A et al(2011) [(22)] had 100% sensitivity and 91.8% specificity and in the study of Mordan 2015 were 94.4%, 100%, and 97.7% for diagnosis of benign condition, which is higher with our result. In this study inadequate specimen was reported in one case 1.3%. Those labelled unsatisfactory for reporting showed fragmented tissue and large areas of hemorrhage. Limited literature is available on the criteria for adequate and inadequate endometrial specimen.

D& C is a useful procedure for diagnosing endometrial abnormalities in women with AUB, Larger size study and equal variables for both perimenopausal and postmenopausal women are essential for this assessment.Experience and knowledge of pathologist that is vital in final diagnosis of results.

In conclusions, there is an age specific association of AUB with increase incidence in perimenopausal age group. Endometrial hyperplasia was the most common cause of AUB, and most of patients were grand muliparous and most common presenting symptom was menorrhagia, Endometrial hyperplasia was the most common histological pattern seen in AUB for a woman in the age of (40-49) years, with least sensitivity and specificity if compared with hysterectomy specimens.

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